

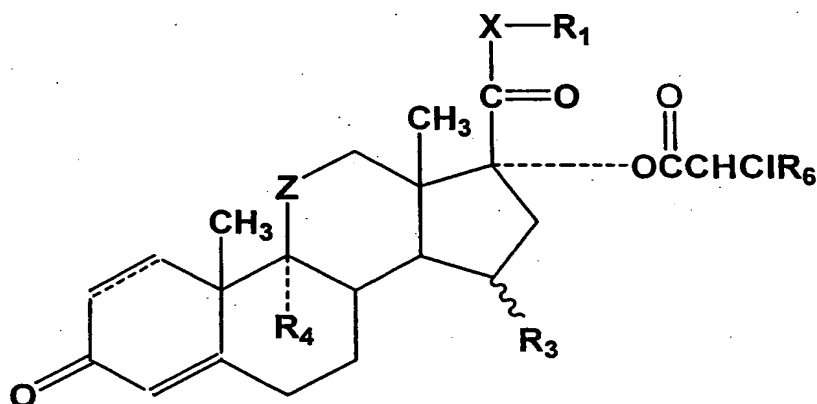
What is claimed is:

1. A composition comprising particles of at least one soft steroid and at least one excipient, wherein said at least one soft steroid particles have a volume mean diameter of less than about 20 micrometers and said at least one excipient particles have a volume mean diameter in the range of about 10 to about 1000 micrometers.
2. A composition as claimed in claim 1, wherein the volume mean diameter of the soft steroid particles is less than the mean diameter of the excipient particles.
3. A composition as claim 2, wherein the volume mean diameter of the soft steroid particles is more than about 3 times smaller than the mean diameter of the excipient particles.
4. A composition as claimed in claim 3, wherein the volume mean diameter of the soft steroid particles is more than 5 times smaller than the mean diameter of the excipient particles.
5. A composition as claimed in any one of the preceding claims, wherein at least 50 wt% of the soft steroid particles have a diameter less than about 10  $\mu\text{m}$ .
6. A composition as claimed in claim 5, wherein at least 50 wt% of the soft steroid particles have a diameter less than about 5  $\mu\text{m}$ .
7. A composition as claimed in claim 6, wherein at least 50 wt% of the soft steroid particles have a diameter less than about 3  $\mu\text{m}$ .
8. A composition as claimed in claim 8, wherein at least 90 wt% of the soft steroid particles have a diameter of less than about 3  $\mu\text{m}$ .
9. A composition as claimed in any one of the preceding claims, wherein the volume mean diameter of the said soft steroid particles is less than about 10  $\mu\text{m}$ .
10. A composition as claimed in claim 8, wherein said soft steroid particles have an average volume mean diameter of about 5  $\mu\text{m}$  or less.

11. A composition as claimed in claim 9, wherein said soft steroid particles have an average volume mean diameter from about 0.5 to about 5  $\mu\text{m}$ .
12. A composition as claimed in claim 10, wherein said soft steroid particles have an average volume mean diameter from about 1.5 to about 3  $\mu\text{m}$ .
- 5 13. A composition as claimed in any one of the preceding claims, wherein said excipient particles have an average volume mean diameter in the range from about 15 to about 250 micrometers.
14. A as claimed in claim 12, wherein said excipient particles have an average volume mean diameter in the range of about 20 to about 100 micrometers.
- 10 15. A composition as claimed in any one of the preceding claims, wherein at least about 30 wt% of the excipient particles have a diameter less than 100  $\mu\text{m}$ .
16. A composition as claimed in claim 15, wherein no more than about 50 wt% of the excipient particles have a diameter less than about 10  $\mu\text{m}$ .
- 15 17. A composition as claimed in any one of the preceding claims, wherein at least about 50 wt% of the excipient particles have a diameter less than 500  $\mu\text{m}$ .
18. A composition as claimed in any one of the preceding claims, wherein said composition is a dry homogenous blend.
19. A composition as claimed in any one of the preceding claims, wherein said composition is formed by mixing of the soft steroid and excipient particles.
- 20 20. A composition as claimed in any one of the preceding claims, wherein the concentration of said soft steroid particles is up to about 50% by wt in relation to the excipient particles.
21. A composition as claimed in claim 20, wherein the concentration of said soft steroid particles is in the range of about 1 to about 10 percent by wt in relation to the excipient particles.

22. A composition as claimed in claim 21, wherein the concentration of said soft steroid particles is in the range of about 3 to about 7 percent by wt in relation to the excipient particles.

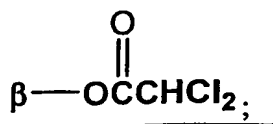
23. A composition as claimed in any one of the preceding claims, wherein said soft steroid is defined by the structural formula:



wherein

R<sub>1</sub> is C<sub>1</sub>-C<sub>4</sub> alkyl, which is unsubstituted or which bears one substituent selected from the group consisting of chloro, fluoro, C<sub>1</sub>-C<sub>4</sub> alkoxy, C<sub>1</sub>-C<sub>4</sub> alkythio, C<sub>1</sub>-C<sub>4</sub> alkylsulfinyl and C<sub>1</sub>-C<sub>4</sub> alkylsulfonyl;

R<sub>3</sub> is hydrogen, α-hydroxy, β-hydroxy, α-methyl, β-methyl =CH<sub>2</sub>, or α or



R<sub>4</sub> is hydrogen; fluoro, or chloro;

R<sub>5</sub> is hydrogen, fluoro, chloro or methyl;

R<sub>6</sub> is hydrogen, chloro or methyl;

X is -O- or -S-;

Z is carbonyl,  $\beta$ -hydroxymethylene or  $\beta$ -chloromethylene;

and the dotted line in ring A indicates that the 1,2-linkage is saturated or unsaturated.

24. A composition as claimed in claim 23, wherein  $R_3$  is H,  $R_4$  is H or F and  $R_5$  is H, F or  $CH_3$ ; or  $R_3$  is  $\alpha$ - $CH_3$  or  $\beta$ - $CH_3$ ,  $R_4$  is H or F and  $R_5$  is H, F or  $CH_3$ ; or  $R_3$  is  $\alpha$ -OH,  $\beta$ -OH,  $\alpha$ -OCOCHCl<sub>2</sub> or  $\beta$ -OCOCHCl<sub>2</sub>,  $R_4$  is H or F and  $R_5$  is H, F or  $CH_3$ .

25. A composition as claimed in claim 23, wherein said soft steroid comprises one or more of the following structural characteristics:

(5)  $R_1$  is unsubstituted  $C_1$ - $C_4$  alkyl or chloromethyl, especially when  $R_1$  is unsubstituted alkyl, most especially when  $R_1$  is ethyl or methyl;

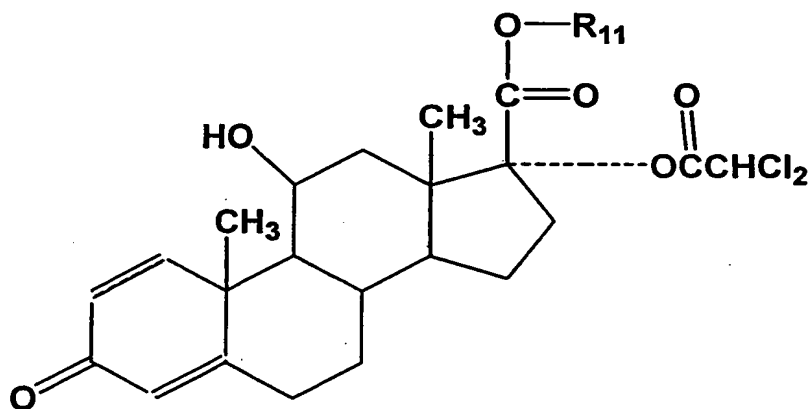
(6) X is -O-;

(7) Z is  $\beta$ -hydroxymethylene;

the 1,2-linkage is unsaturated; and

(4)  $R_6$  is Cl.

26. A composition as claimed in claim 23, wherein said soft steroid is defined by the structural formula:

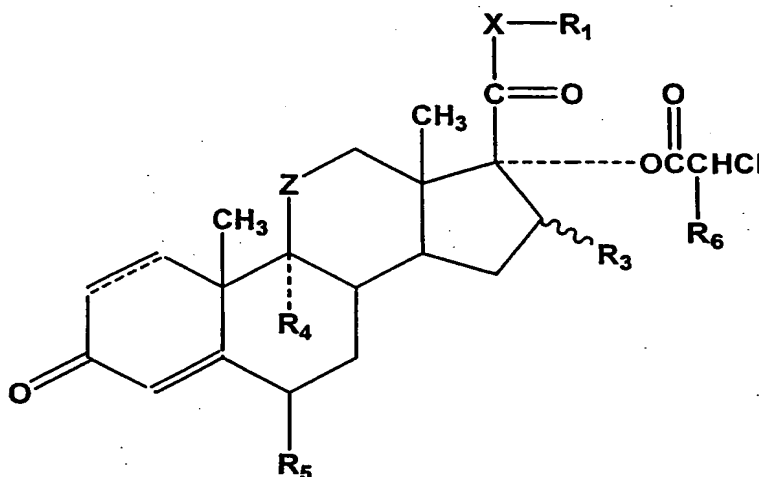


wherein  $R_{11}$  is methyl, ethyl, isopropyl or chloromethyl, especially when  $R_{11}$  is methyl, ethyl or isopropyl.

27. A composition as claimed in any one of the preceding claims, wherein said soft steroid is etiprednol dicloacetate.

28. A composition as claimed in any one of the preceding claims, wherein said soft steroid is loteprednol etabonate.

29. A composition as claimed in claim 23, wherein said soft steroid is defined by the structural formula:

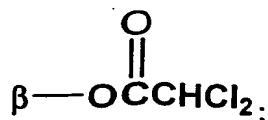


10 wherein

$R_6$  is H or  $CH_3$ , particularly when  $R_6$  is  $CH_3$ ,

$R_1$  is  $C_1$ - $C_4$  alkyl, which is unsubstituted or which bears one substituent selected from the group consisting of chloro, fluoro,  $C_1$ - $C_4$  alkoxy,  $C_1$ - $C_4$  alkythio,  $C_1$ - $C_4$  alkylsulfinyl and  $C_1$ - $C_4$  alkylsulfonyl;

15  $R_3$  is hydrogen,  $\alpha$ -hydroxy,  $\beta$ -hydroxy,  $\alpha$ -methyl,  $\beta$ -methyl  $=CH_2$ , or  $\alpha$ - or



R<sub>4</sub> is hydrogen; fluoro, or chloro;

R<sub>5</sub> is hydrogen; fluoro, chloro or methyl;

X is -O- or -S-;

5 Z is carbonyl, β-hydroxymethylene or β-chloromethylene;

and the dotted line in ring A indicates that the 1,2-linkage is saturated or unsaturated.

30. A composition as claimed in claim 23, wherein the soft steroid comprises the following sub-groups

(4) compounds in which R<sub>3</sub> is H, R<sub>4</sub> is H or F and R<sub>5</sub> is H, F or CH<sub>3</sub>; or

10 (5) compounds in which R<sub>3</sub> is α-CH<sub>3</sub> or β-CH<sub>3</sub>, R<sub>4</sub> is H or F and R<sub>5</sub> is H, F or CH<sub>3</sub>; or

(6) R<sub>3</sub> is α-OH, β-OH, α-OCOCHCl<sub>2</sub> or β-OCOCHCl<sub>2</sub>, R<sub>4</sub> is H or F and R<sub>5</sub> is H, F or CH<sub>3</sub>.

31. A composition as claimed in claim 23, wherein the soft steroid comprises one or more of the following structural characteristics

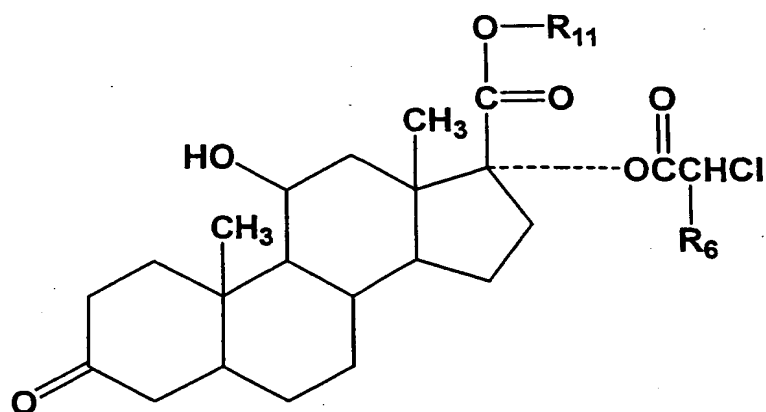
15 (6) R<sub>1</sub> is unsubstituted C<sub>1</sub>-C<sub>4</sub> alkyl or chloromethyl, especially when R<sub>1</sub> is unsubstituted alkyl, most especially when R<sub>1</sub> is ethyl or methyl;

(7) X is -O-;

(8) Z is β-hydroxymethylene;

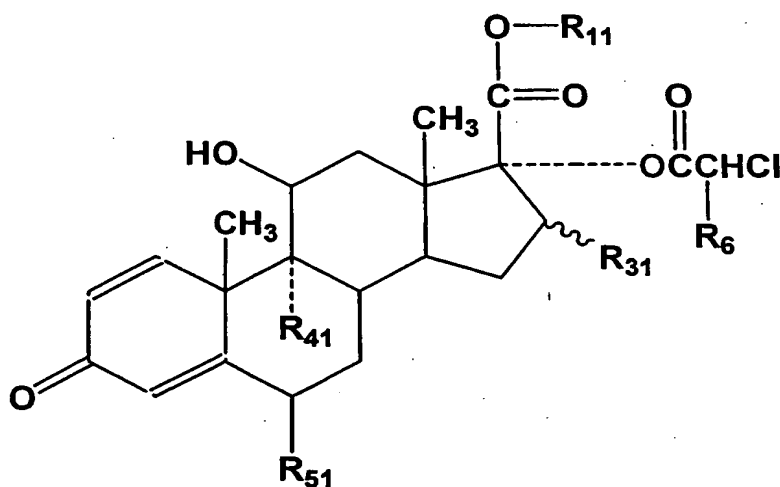
the 1,2-linkage is unsaturated.

20 32. A composition as claimed in claim 23, wherein said soft steroid is defined by the structural formula:



wherein  $R_{11}$  is methyl, ethyl, isopropyl or chloromethyl, and  $R_6$  is H or  $CH_3$ , especially when  $R_{11}$  is methyl, ethyl or isopropyl.

33. A composition as claimed in claim 23, wherein said soft steroid is defined by the structural formula:



wherein  $R_{11}$  is methyl, ethyl, isopropyl or chloromethyl,  $R_{31}$  is  $\alpha$ - $CH_3$  or  $\beta$ - $CH_3$ ,  $R_{41}$  is H or F,  $R_{51}$  is H or F,  $R_6$  is H or  $CH_3$ , especially when  $R_{11}$  is methyl, ethyl or isopropyl.

34. A composition as claimed in any one of the preceding claims, wherein said excipient comprises one or more of lactose, sucrose, glucose, mannitol, xylitol, trehalose, or other monosaccharides, disaccharides or polysaccharides, or derivatives thereof.

35. A composition as claimed in claim 34, wherein said excipient is lactose monohydrate.

36. A medicament suitable for use in a dry powder inhaler comprising particles of at least one soft steroid and at least one excipient, wherein said at least one soft steroid particles have a volume mean diameter of less than about 20 micrometers and said at least one excipient  
5 particles have a volume mean diameter in the range of about 10 to about 1000 micrometers.

37. A medicament as claimed in claim 36, wherein the volume mean diameter of the soft steroid particles is less than the mean diameter of the excipient particles.

38. A medicament as claim 37, wherein the volume mean diameter of the soft steroid  
10 particles is more than about 3 times smaller than the mean diameter of the excipient particles.

39. A medicament as claimed in claim 38, wherein the volume mean diameter of the soft steroid particles is more than 5 times smaller than the mean diameter of the excipient particles.

15 40. A medicament as claimed in claim 36, wherein at least 50 wt% of the soft steroid particles have a diameter less than about 10  $\mu\text{m}$ .

41. A medicament as claimed in claim 40, wherein at least 50 wt% of the soft steroid particles have a diameter less than about 5  $\mu\text{m}$ .

20 42. A medicament as claimed in claim 41, wherein at least 50 wt% of the soft steroid particles have a diameter less than about 3  $\mu\text{m}$ .

43. A medicament as claimed in claim 42, wherein at least 90 wt% of the soft steroid particles have a diameter of less than about 3  $\mu\text{m}$ .

44. A medicament as claimed in claim 36, wherein the volume mean diameter of the said soft steroid particles is less than about 10  $\mu\text{m}$ .

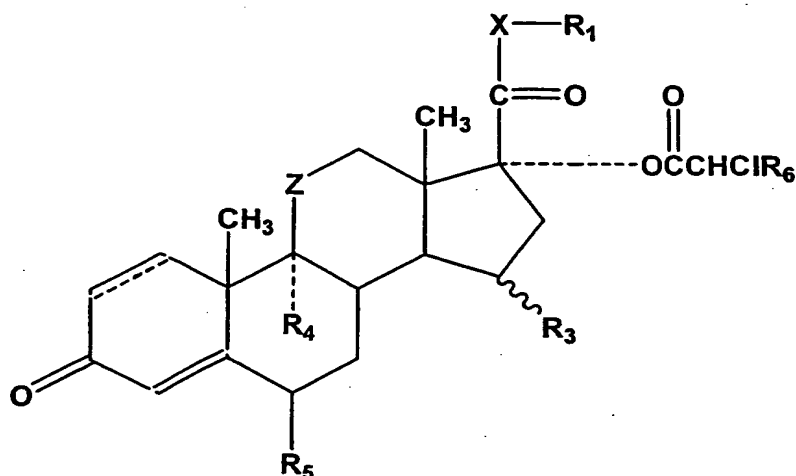
25 45. A medicament as claimed in claim 44, wherein said soft steroid particles have a volume mean diameter of about 5  $\mu\text{m}$  or less.



46. A medicament as claimed in claim 45, wherein said soft steroid particles have a volume mean diameter from about 0.5 to about 5  $\mu\text{m}$ .
47. A medicament as claimed in claim 55, wherein said soft steroid particles have a volume mean diameter from about 1.5 to about 3  $\mu\text{m}$ .
- 5 48. A medicament as claimed in claim 36, wherein said excipient particles have a volume mean diameter in the range from about 15 to about 250 micrometers.
49. A medicament as claimed in claim 48, wherein said excipient particles have a volume mean diameter in the range of about 20 to about 100 micrometers.
- 10 50. A medicament as claimed in claim 36, wherein at least about 30 wt% of the excipient particles have a diameter less than 100  $\mu\text{m}$ .
51. A medicament as claimed in claim 50, wherein no more than about 50 wt% of the excipient particles have a diameter less than about 10  $\mu\text{m}$ .
52. A medicament as claimed in claim 36, wherein at least about 50 wt% of the excipient particles have a diameter less than 500  $\mu\text{m}$ .
- 15 53. A medicament as claimed in claim 36, wherein said medicament comprises or consists of a dry homogenous blend of said soft steroid particles and said excipient particles.
54. A medicament as claimed in claim 53, wherein said medicament is formed by mixing of the soft steroid and excipient particles.
- 20 55. A medicament as claimed in claim 36, wherein the concentration of said soft steroid particles is up to about 50% by wt in relation to the excipient particles.
56. A medicament as claimed in claim 55, wherein the concentration of said soft steroid particles is in the range of about 1 to about 10 percent by wt in relation to the excipient particles.

57. A medicament as claimed in claim 56, wherein the concentration of said soft steroid particles is in the range of about 3 to about 7 percent by wt in relation to the excipient particles.

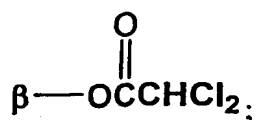
58. A medicament as claimed in claim 36, wherein said soft steroid is defined by the structural formula:



wherein

10  $R_1$  is  $C_1$ - $C_4$  alkyl, which is unsubstituted or which bears one substituent selected from the group consisting of chloro, fluoro,  $C_1$ - $C_4$  alkoxy,  $C_1$ - $C_4$  alkythio,  $C_1$ - $C_4$  alkylsulfinyl and  $C_1$ - $C_4$  alkylsulfonyl;

$R_3$  is hydrogen,  $\alpha$ -hydroxy,  $\beta$ -hydroxy,  $\alpha$ -methyl,  $\beta$ -methyl  $=CH_2$ , or  $\alpha$  or



$R_4$  is hydrogen, fluoro, or chloro;

$R_5$  is hydrogen, fluoro, chloro or methyl;

15  $R_6$  is hydrogen, chloro or methyl;

X is -O- or -S-;

Z is carbonyl,  $\beta$ -hydroxymethylene or  $\beta$ -chloromethylene;

and the dotted line in ring A indicates that the 1,2-linkage is saturated or unsaturated.

59. A medicament as claimed in claim 58, wherein

5      $R_3$  is H,  $R_4$  is H or F and  $R_5$  is H, F or  $CH_3$ ; or

$R_3$  is  $\alpha$ - $CH_3$  or  $\beta$ - $CH_3$ ,  $R_4$  is H or F and  $R_5$  is H, F or  $CH_3$ ; or

$R_3$  is  $\alpha$ -OH,  $\beta$ -OH,  $\alpha$ -OCOCHCl<sub>2</sub> or  $\beta$ -OCOCHCl<sub>2</sub>,  $R_4$  is H or F and  $R_5$  is H, F or  $CH_3$ .

60. A medicament as claimed in claim 59, wherein said soft steroid comprises one or more of the following structural characteristics:

10      $R_1$  is unsubstituted  $C_1$ - $C_4$  alkyl or chloromethyl, especially when  $R_1$  is unsubstituted alkyl, most especially when  $R_1$  is ethyl or methyl;

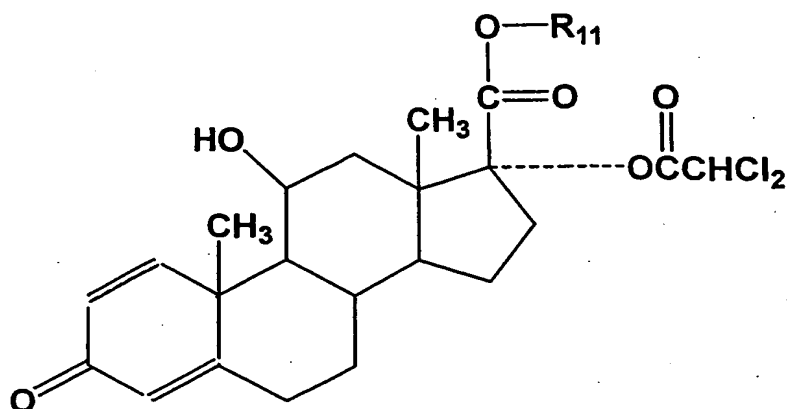
X is -O-;

Z is  $\beta$ -hydroxymethylene;

the 1,2-linkage is unsaturated; and

15      $R_6$  is Cl.

61. A medicament as claimed in claim 58, wherein said soft steroid is defined by the structural formula:

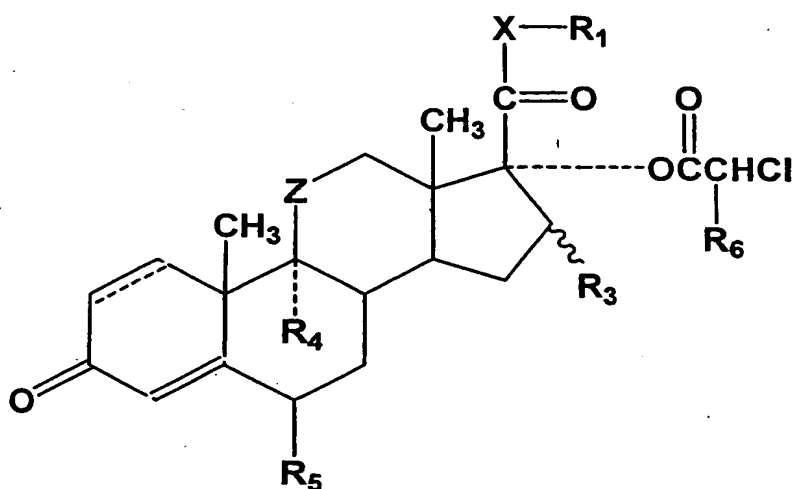


wherein  $R_{11}$  is methyl, ethyl, isopropyl or chloromethyl, especially when  $R_{11}$  is methyl, ethyl or isopropyl.

62. A medicament as claimed in claim 36, wherein said soft steroid is etiprednol dicloacetate.

5 63. A medicament as claimed in claim 36, wherein said soft steroid is loteprednol etabonate.

64. A medicament as claimed in claim 58, wherein said soft steroid is defined by the structural formula:

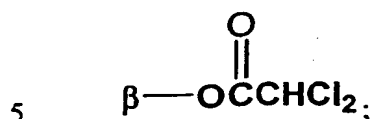


wherein

10  $R_6$  is H or  $CH_3$ , particularly when  $R_6$  is  $CH_3$ ,

R<sub>1</sub> is C<sub>1</sub>-C<sub>4</sub> alkyl, which is unsubstituted or which bears one substituent selected from the group consisting of chloro, fluoro, C<sub>1</sub>-C<sub>4</sub> alkoxy, C<sub>1</sub>-C<sub>4</sub> alkythio, C<sub>1</sub>-C<sub>4</sub> alkylsulfinyl and C<sub>1</sub>-C<sub>4</sub> alkylsulfonyl;

R<sub>3</sub> is hydrogen, α-hydroxy, β-hydroxy, α-methyl, β-methyl =CH<sub>2</sub>, or α or



R<sub>4</sub> is hydrogen; fluoro, or chloro;

R<sub>5</sub> is hydrogen; fluoro, chloro or methyl,

X is -O- or -S-;

Z is carbonyl, β-hydroxymethylene or β-chloromethylene;

10      and the dotted line in ring A indicates that the 1,2-linkage is saturated or unsaturated.

65. A medicament as claimed in claim 58, wherein the soft steroid comprises the following sub-groups compounds in which R<sub>3</sub> is H, R<sub>4</sub> is H or F and R<sub>5</sub> is H, F or CH<sub>3</sub>; or

compounds in which R<sub>3</sub> is α-CH<sub>3</sub> or β-CH<sub>3</sub>, R<sub>4</sub> is H or F and R<sub>5</sub> is H, F or CH<sub>3</sub>; or

R<sub>3</sub> is α-OH, β-OH, α-OCOCHCl<sub>2</sub> or β-OCOCHCl<sub>2</sub>, R<sub>4</sub> is H or F and R<sub>5</sub> is H, F or CH<sub>3</sub>.

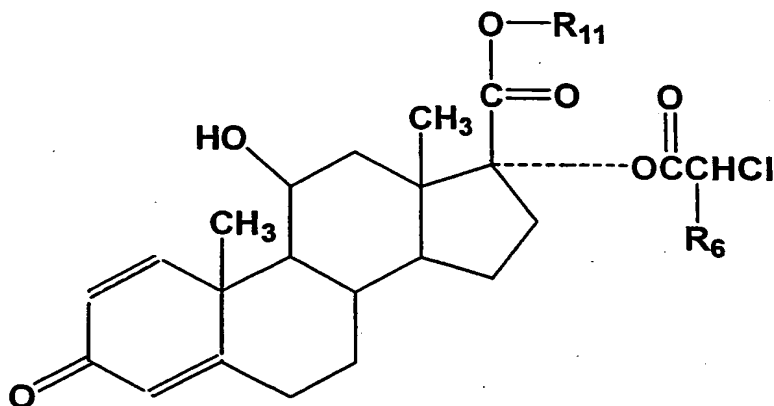
15      66. A medicament as claimed in claim 58, wherein the soft steroid comprises one or more of the following structural characteristics R<sub>1</sub> is unsubstituted C<sub>1</sub>-C<sub>4</sub> alkyl or chloromethyl, especially when R<sub>1</sub> is unsubstituted alkyl, most especially when R<sub>1</sub> is ethyl or methyl;

X is -O-;

Z is β-hydroxymethylene;

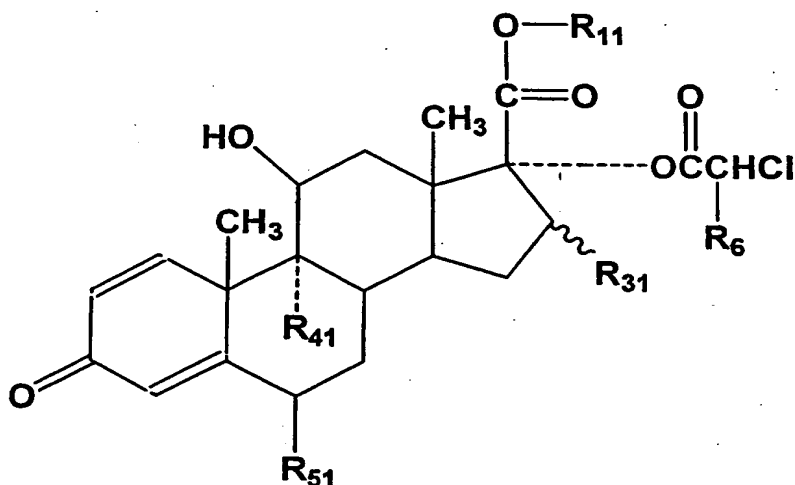
20      the 1,2-linkage is unsaturated.

67. A medicament as claimed in claim 58, wherein said soft steroid is defined by the structural formula:



wherein  $R_{11}$  is methyl, ethyl, isopropyl or chloromethyl, and  $R_6$  is H or  $CH_3$ , especially when  $R_{11}$  is methyl, ethyl or isopropyl.

68. A medicament as claimed in claim 58, wherein said soft steroid is defined by the structural formula:



wherein  $R_{11}$  is methyl, ethyl, isopropyl or chloromethyl,  $R_{31}$  is  $\alpha$ - $CH_3$  or  $\beta$ - $CH_3$ ,  $R_{41}$  is H or F,  $R_{51}$  is H or F,  $R_6$  is H or  $CH_3$ , especially when  $R_{11}$  is methyl, ethyl or isopropyl.

69. A medicament as claimed in claim 36, wherein said excipient comprises one or more of lactose, sucrose, glucose, mannitol, xylitol, trehalose, or other monosaccharides, disaccharides or polysaccharides, or derivatives thereof.

70. A medicament as claimed in claim 36, wherein said excipient is lactose monohydrate.

5 71. A medicament comprising the composition of claim 1.

72. A medicament suitable for use in a dry powder inhaler comprising the composition as claimed in claim 1.

10 73. A method of preparing a medicament as claimed in claim 36, wherein said method comprises admixing particles of said soft steroid and said excipient under shear or kinetic mixing conditions.

15 74. A method of treating a mammal with a medicament administered by way of a dry powder inhaler, said medicament comprising particles of at least one soft steroid and at least one excipient, wherein said at least one soft steroid particles have a volume mean diameter of less than about 20 micrometers and said at least one excipient particles have a volume mean diameter in the range of about 10 to about 1000 micrometers.

75. The method according to claim 74, wherein the medicament is administered for the treatment of respiratory tract or lung based diseases or disorders in mammals, such as asthma.

20 76. The method according to claim 74, wherein the medicament delivers a dose of about 10 to about 5000 micrograms of soft steroid to said mammal.

77. The method according to claim 74, wherein the medicament delivers a dose of about 100 to about 500 micrograms of soft steroid to said mammal.

78. The method according to claim 74, wherein the medicament delivers a a dose of about 200 micrograms of soft steroid to said mammal.

25 79. The use of a composition comprising particles of at least one soft steroid and at least one excipient, wherein said at least one soft steroid particles have a volume mean diameter of

less than about 20 micrometers and said at least one excipient particles have a volume mean diameter in the range of about 10 to about 1000 micrometers in the preparation of a medicament for the treatment of respiratory tract or lung diseases or disorders in a mammal.

- 5 80. The use as claimed in claim 79, wherein the medicament is for the treatment of asthma.
81. A medicament according to claim 36 in which the presence of said excipient improves the stability of the soft steroid.